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Title: Long-term bortezomib treatment decreases allergen-specific IgE but fails to amend chronic asthma in mice

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Body: Since allergen-specific immuno-globulin E (IgE) enables mast cells and eosinophils to react on allergen-contact it plays a critical role in the formation of allergic inflammation and has been identified as a target for asthma therapy. By inhibiting the proteasome complex Bortezomib efficiently depletes Ig-secreting plasma cells and, thus, reduces Ig-serum titers. The present study evaluates the therapeutic potential of Bortezomib in a mouse model of chronic experimental asthma. Therefore, BALB/c mice were sensitized to ovalbumin (OVA) and challenged with OVA-aerosol for twelve weeks. Bortezomib treatment was started after six weeks of challenge, and continued for one week (short-term) or six weeks (long-term), respectively, with a dosage of 0.75 mg/kg body weight with two intra-venous injections weekly. Airway responsiveness to metacholine, lung histology, Ig serum titers, and plasma cell numbers were assessed. In mice with chronic experimental asthma short-term treatment resulted in decreased eosinophil numbers in BAL fluids, while long-term treatment significantly lowered serum titers of anti-OVA IgE. Nevertheless, neither short-term nor long-term treatment significantly diminish ed plasma cell numbers, anti-OVA IgG1 serum titers, allergic airway inflammation or improved lung function. These results demonstrate that Bortezomib has no therapeutic effect on chronic experimental asthma in mice. Therefore, Bortezomib treatment could have only limited value as plasma cell depleting therapy against allergic bronchial asthma.